

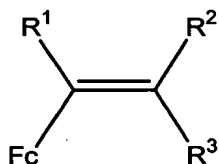
Method for the preparation of ferrocenyl substituted styrene

Field of the Invention

The present invention relates to a method for manufacturing ferrocenyl substituted styrene. More particularly, the present invention relates to a method
5 for manufacturing ferrocenyl substituted styrene without heating or vacuum sublimation.

Background of the Invention

A ferrocenyl double bond compound having the following structure can be
10 utilized in various applications:

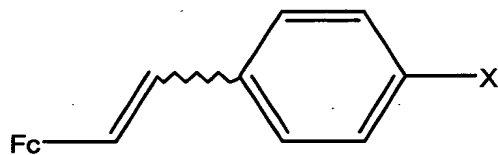


wherein Fc is ferrocenyl, for examples the applications disclosed in FR
2,567,890 (1986), U.S. Pat. 4,219,490 (1980) and Czech. 175,857 (1979). C. A.
90,138026c discloses that a ferrocenyl ethylene compound can be used to
15 synthesize ferrocenyl derivatives.

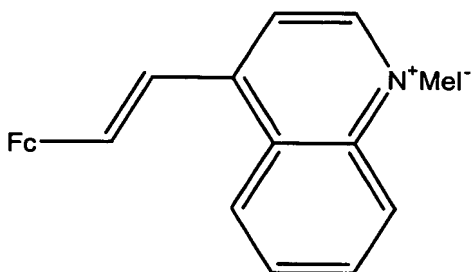
JP 7-309915 (1995) discloses a high refractive index resin of a
polyvinylferrocene copolymer.

JP 8-029372 (1996) discloses an enzyme electrode made from a copolymer
of a vinyl monomer having a ferrocene and dodecyl methacrylate.

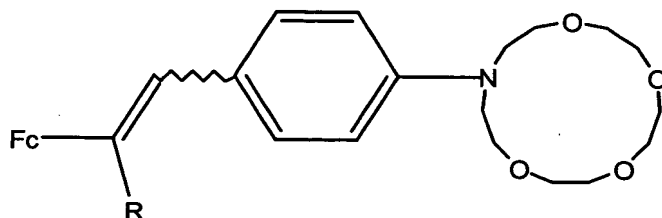
20 An article, Nature 330,360 (1987), discloses that the following compound
has non-linear optical properties:



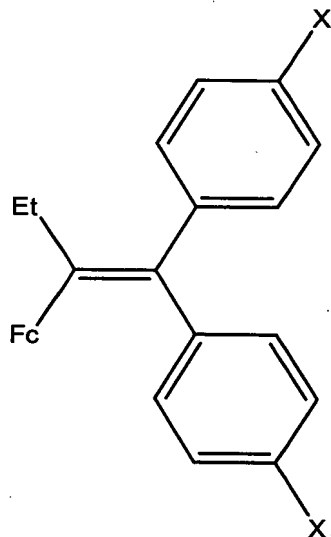
Another article, Inorg Chim. Acta, 242(1-2), 43 (1996), discloses a
25 non-linear optical compound having the following structure:



A further article, J. Chem. Soc., Chem. Commun., 1122 (1987), discloses redox-active crown ethers having the following structure:

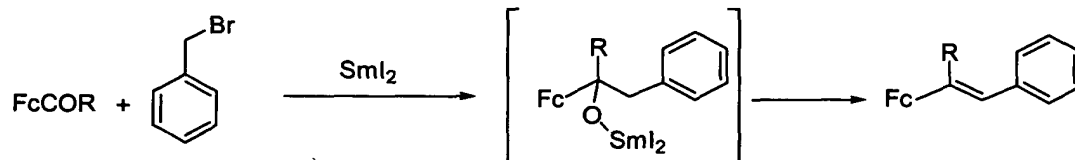


- 5 WO 96/11935 (1996) discloses compounds having the following structure, the methods of preparation and pharmaceutical compositions containing same:



- The derivatives of this patent application are suitable for the preparation of antitumoral drugs for use, in particular, in the treatment of estrogen-dependent
10 breast cancers.

An article, J. Org. Chem., 66, 3533 (2001), discloses a method for synthesizing ferrocenyl styrene by reacting ferrocenecarbonyl and toluene bromide, the reaction of which can be represented as follows:



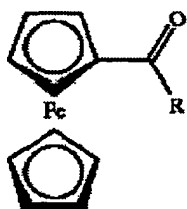
In this method the reaction is carried out in tetrahydrofuran (THF) and in the presence of samarium diiodide as a catalyst, and then the reaction mixture is dehydrated under reflux in air to obtain ferrocenyl styrene. The catalyst used, samarium diiodide, is expensive and will undergo hydrolysis in air or moisture.

US patent No. 6,211,392B1 discloses a method of manufacturing ferrocenyl-1,3-butadiene, in which a ferrocenecarbonyl is reacted with an allyl halide in a polar aprotic solvent lacking a carbonyl group in the presence of samarium diiodide as a catalyst. The method of this US patent has a relatively high yield; however, the catalyst used, samarium diiodide, is expensive and will undergo hydrolysis in air or moisture.

There is still a need in the industry for developing an easier method for the preparation of ferrocenyl styrene.

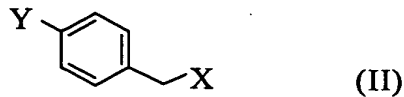
Summary of the Invention

The present invention provides a method for synthesizing ferrocenyl substituted styrene having the following Formula III, which comprises: a) reacting ferrocenecarbonyl having the following Formula I with toluene halide having the following Formula II in an ether solvent and in the presence of magnesium as a catalyst; b) introducing a liquid portion of the resulting reaction mixture into a silica gel column; c) eluting the silica gel column with a solvent of low polarity; d) collecting the resulting eluate from the column; e) and evaporating the solvent from the eluate to obtain a solid comprising ferrocenyl substituted styrene (III):

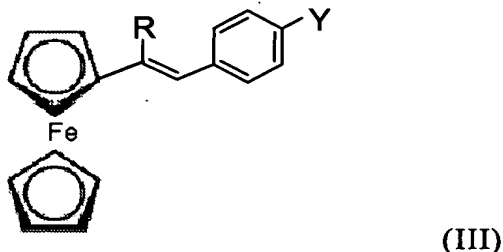


(I)

wherein R is hydrogen or C1-C4 alkyl;



wherein X is a halogen; Y is a halogen, hydrogen or C1-C4 alkyl;



wherein R and Y are defined as above.

5 Preferably, X is bromine, and Y is hydrogen or C1-C4 alkyl.

Preferably, R is hydrogen or methyl.

Preferably, the ether solvent is tetrahydrofuran or ethyl ether, and more preferably, tetrahydrofuran.

10 Preferably, said solvent of low polarity is n-hexane, ethyl acetate or a mixture of them.

Preferably, said reaction in step a) is carried out at room temperature for a period of 3-48 hours.

Preferably, said liquid portion is kept in the silica gel column for a period of 6-96 hours in step b).

15 Preferably, a mole ratio of said toluene halide (II) to said ferrocenecarbonyl (I) in said reaction in step a) ranges from 0.1 to 20, and more preferably, is about 1.5.

Preferably, a mole ratio of said magnesium catalyst to said ferrocenecarbonyl (I) in said reaction in step a) ranges from 0.1 to 20, and more preferably, is about 3.

20

In the method of the present invention, the reaction mixture in step a) does not need to be heated under refluxing, and the catalyst used is a common alkaline earth metal.

25 Detailed Description of the Invention

A synthesis method for ferrocenyl substituted styrene according to one of the

preferred embodiments of the present invention can be represented by the following reaction formula:



5 wherein Fc is ferrocenyl, Y and R are defined as above.

Ferrocenecarbonyl (I) reacts with toluene bromide (II) having a substituent, Y, in the presence of magnesium metal as a catalyst and in an ether solvent such as tetrahydrofuran (THF). The liquid portion of the reaction mixture is introduced into a silica gel column, and is kept in the silica gel
 10 column for a certain period of time such that the silica gel having a weak acidity dehydrates the reaction intermediate, ferrocenyl alcohol, into ferrocenyl substituted styrene (III) having a lower polarity. Next, an eluent having a low polarity such as n-hexane, ethyl acetate or a mixture thereof is used to desorb the product (III), and the eluate is collected. After removing the solvent by
 15 evaporation, a purified ferrocenyl substituted styrene product is obtained. The silica gel used in the present invention is not limited and can be an arbitrary commercial silica gel. The invented method is simple to be operated and requires no refluxing or vacuuming. Moreover, the catalyst used is stable and is not expensive.

20 In the method of the present invention, a suitable amount of the ether solvent for in the reaction is 1-20 liters, and preferably is about 15 liters, per mole of the ferrocenecarbonyl (I).

The present invention can be further elaborated by way of the following examples which are for illustrative purposes only and not for limiting the scope
 25 of the present invention.

Example 1: Synthesis of 1-ferrocenyl-1-methyl,2-styrene

72 mg (3.0 mmole) of magnesium metal was placed in a 50 ml round bottom flask. 228 mg (1.0 mmole) of ferrocenyl methyl ketone and 256.5 mg

(1.5 mmole) of toluene bromide were dissolved in 15 ml of THF. The resulting mixture was poured into the round bottom flask containing the magnesium metal while stirring at room temperature for 12 hours. After 12-hour stirring, the cover of the flask was opened, and the liquid portion of the reaction mixture was introduced into a silica gel column, which had been wetted with n-hexane. All the liquid migrated into the silica gel, and the column was placed still for 48 hours. Next, the column was eluted with a mixed solvent of ethyl acetate and n-hexane (1:4 by volume). After evaporating the solvent from the eluate collected from the elution, 275 mg (0.91 mmole) of a purified title product was obtained with a yield of 91%.

Melting poitn: 64~66°C

$^1\text{H-NMR}(\text{CDCl}_3) \delta :$

2.13(3H, s)

4.05(5H, s)

15 4.18(2H, s)

4.39(2H, s)

6.64(1H, s)

7.26~7.10(5H, m)

IR(KBr) :1627 cm^{-1}

20 FAB-MS m/z 302(M^+)

Example 2: Synthesis of 1-ferrocenyl, 2-styrene

72 mg (3.0 mmole) of magnesium metal was placed in a 50 ml round bottom flask. 214 mg (1.0 mmole) of ferrocenyaldehyde and 256.5 mg (1.5 mmole) of toluene bromide were dissolved in 15 ml of THF. The resulting mixture was poured into the round bottom flask containing the magnesium metal while stirring at room temperature for 12 hours. After 12-hour stirring, the cover of the flask was opened, and the liquid portion of the reaction mixture was introduced into a silica gel column, which had been wetted with n-hexane. All the liquid migrated into the silica gel, and the column was placed still for 48 hours. Next, the column was eluted with a mixed solvent of ethyl acetate and

n-hexane (1:4 by volume). After evaporating the solvent from the eluate collected from the elution, 232 mg (0.80 mmole) of a purified title product was obtained with a yield of 80%.

Melting point: 118°C

5 $^1\text{H-NMR}(\text{CDCl}_3) \delta :$

4.16(5H, s)

4.30(2H, t)

4.49(2H, t)

6.72(1H, d)

10 6.90(1H, d)

7.47~7.22(5H, m)

IR(KBr) :1636, 1597 cm^{-1}

FAB-MS m/z 288(M^+)

15